SEQUENCE LISTING

<110> Huang, Shi Chadwick, Robert B.

<120> Methods of Detecting and Treating Microsatellite-Instability Positive Tumors Using RIZ

<130> P-LJ 5101

<150> US 60/256,582

<151> 2000-12-19

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tet gtg gca gcc act gag act ctg gct gag gta cct gaa cat gtg ctt 222 Ser Val Ala Ala Thr Glu Thr Leu Ala Glu Val Pro Glu His Val Leu 15 10

cga gga ctt cca gag gaa gta aga ctt ttc cca tct gca gtc gac aag 270 Arg Gly Leu Pro Glu Glu Val Arg Leu Phe Pro Ser Ala Val Asp Lys 30 25

act cgg att ggt gtc tgg gct act aaa cca att tta aaa ggg aaa aag 318 Thr Arg Ile Gly Val Trp Ala Thr Lys Pro Ile Leu Lys Gly Lys Lys 45 40

ttt ggg cca ttt gtt ggt gat aag aag aga tcc cag gtt agg aat 366 Phe Gly Pro Phe Val Gly Asp Lys Lys Lys Arg Ser Gln Val Arg Asn 65 60 55

aat gtg tac atg tgg gag gtc tac tac cca aat ttg ggg tgg atg tgc Asn Val Tyr Met Trp Glu Val Tyr Tyr Pro Asn Leu Gly Trp Met Cys

I,M ļ.± ľIJ -ايـ" 1 -

75 80 85

| - | gcc acc Ala Thr 90 | _ | | _ | _ | | | | | 462 |
|---|---------------------------|--------|-------|---|---|---|---|---|---|---------|
| | tgc tca Cys Ser 105 | | | | | | | | | 510 |
| | att tac Ile Tyr | | | | _ | | | | | 558 |
| | gtc tgg Val Trp | | n Gly | | | | | | | 606 |
| | gaa gag Glu Glu | | _ | - | | _ | | | | 654 |
| | aga ggg Arg Gly 170 | | | | | | | | | 702 |
| | cac ccc His Pro 185 | | | | | | | | | 750 |
| _ | atg agg Met Arg | | _ | _ | | | | | | 798 |
| _ | gct tcg Ala Ser | • | o Glu | _ | | _ | _ | _ | | 846 |
| | gat gca Asp Ala | _ | _ | | - | | | _ | _ | 894 |
| | cca gag Pro Glu 250 | Val As | | | | | | | | 942 |
| | gtg gag Val Glu 265 | | | | | | | | | 990 |
| | gag gag Glu Glu | | | | | | | | | 1038 |

| ccg aat (Pro Asn (295 | | | | | | | | | | | 1086 |
|-------------------------------|---|---|-----|---|---|---|---|---|---|---|------|
| cca gaa g Pro Glu | _ | _ | | | - | | _ | _ | _ | _ | 1134 |
| gaa gac Glu Asp | | | | | | | | | | | 1182 |
| gag gag Glu Glu | _ | | Val | | | | | | | | 1230 |
| cac tgt His Cys 360 | | | - | _ | _ | _ | | | | | 1278 |
| cac atc His Ile 375 | | | | | | | | | | | 1326 |
| ggg aaa Gly Lys | | | _ | | | | | | | | 1374 |
| cac gaa His Glu | | | | | | | | | | | 1422 |
| gag gat Glu Asp | - | | | | | | | | | | 1470 |
| tca agt Ser Ser 440 | | | | | | | | | | | 1518 |
| aaa acc Lys Thr 455 | | | | | | | | | | | 1566 |
| gaa gtt Glu Val | - | | _ | _ | | | | | | | 1614 |
| act cac Thr His | | | | | | | | | | | 1662 |

| | | | | | | | | | | _ | | | | | | | |
|----|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-------------------|-----|------|
| | _ | | | | | - | | _ | | | | | | | gag Glu | | 1710 |
| | n | | | | | | | | | | | | | | gtc Val | | 1758 |
| Se | | | | | | | | | | | | | | | atc Ile | | 1806 |
| _ | | | | _ | | | | - | | | | | | | gac Asp 565 | | 1854 |
| | _ | | _ | | | _ | _ | | | | | | | | gag Glu | | 1902 |
| _ | _ | | | | - | | | | | | | | | | act Thr | | 1950 |
| | al | | | | | | | | | | | | | | tct Ser | | 1998 |
| Tì | | | | | | | | | | | | | | | gag Glu | | 2046 |
| | | | | | | | | | | | | | | | aaa Lys 645 | | 2094 |
| | | | | | | | | | | | | | | | ctg Leu | | 2142 |
| | _ | _ | | | | - | | | | | | | | | aag Lys | | 2190 |
| _ | al | | _ | _ | | _ | | _ | _ | | | _ | | _ | gac Asp | - | 2238 |
| Le | | | | | | | | | | | | | | | tta Leu | | 2286 |
| C | CC | gtg | tgc | gcg | tct | gct | cct | gca | tcc | atg | ttg | ccc | gtg | acc | tct | agt | 2334 |

| Pro | Val | Cys | Ala | Ser 715 | Ala | Pro | Ala | Ser | Met 720 | Leu | Pro | Val | Thr | Ser 725 | Ser | |
|-----|-----|-----|----------|------------|-----|-------------------|-----|-----|------------|-----|-----|-----|-----|------------|-----|------|
| | | _ | _ | _ | | agc Ser | | | _ | _ | | | _ | | _ | 2382 |
| | _ | | _ | _ | | gly ggg | | | | _ | | | _ | _ | | 2430 |
| | _ | | _ | _ | | tcc Ser 765 | _ | | | - | | _ | _ | _ | _ | 2478 |
| _ | | | | | - | ttg Leu | | | | | | | _ | | | 2526 |
| _ | | | _ | | _ | gaa Glu | | | | | _ | _ | | _ | _ | 2574 |
| _ | | | | _ | - | gtg Val | _ | | | _ | | _ | _ | | | 2622 |
| _ | | _ | | _ | _ | tca Ser | | | | | _ | | | _ | | 2670 |
| | _ | | _ | _ | _ | ctc Leu 845 | _ | | | | _ | | _ | _ | | 2718 |
| | | _ | - | _ | | gag Glu | | _ | _ | | | | | | _ | 2766 |
| _ | | | | | | tgt Cys | _ | | | _ | _ | | | | | 2814 |
| | | | _ | - | | cct Pro | | - | | | | | | | | 2862 |
| _ | | _ | | _ | | tcc Ser | | _ | | _ | | | | | | 2910 |
| | | _ | | _ | _ | tca Ser | _ | | | _ | | | | | - | 2958 |

gtt gtt ggc cct tcc tca ccc cct ctc cag aca gcc tcc tta tcc tcc Val Val Gly Pro Ser Ser Pro Pro Leu Gln Thr Ala Ser Leu Ser Ser ggt cag ctg cct ctc tta acc ccc aca gag cct tct tcc cct ccc Gly Gln Leu Pro Pro Leu Leu Thr Pro Thr Glu Pro Ser Ser Pro Pro ccc tgc cct cct gtg tta act gtt gcc act cca cca cct ccc ctc ctt Pro Cys Pro Pro Val Leu Thr Val Ala Thr Pro Pro Pro Pro Leu Leu cca acc gtc cct ctc tcc cac ccc tct tct gat gcc tcc cct cag cag Pro Thr Val Pro Leu Ser His Pro Ser Ser Asp Ala Ser Pro Gln Gln tgt ccc tct ccg ttc tca aac acc act gct cag tct cct ctt ccc att Cys Pro Ser Pro Phe Ser Asn Thr Thr Ala Gln Ser Pro Leu Pro Ile ctc tcc cca aca gtg tct ccc tct ccc tct ccc att cct cct gta gag Leu Ser Pro Thr Val Ser Pro Ser Pro Ser Pro Ile Pro Pro Val Glu cca ctt atg tct gct tcc cct ggt ccc cca aca ctt tct tcc tcc Pro Leu Met Ser Ala Ala Ser Pro Gly Pro Pro Thr Leu Ser Ser Ser Ser Ser Ser Ser Ser Phe Pro Ser Ser Cys Ser Ser Thr Ser ccc tcc cca ccc cct ctt tca gca gtg tca tct gtg gtt tcc tct ggg Pro Ser Pro Pro Pro Leu Ser Ala Val Ser Ser Val Val Ser Ser Gly gac aac ctg gag gca tct ctg cct gca gta act ttc aaa cag gag gag Asp Asn Leu Glu Ala Ser Leu Pro Ala Val Thr Phe Lys Gln Glu Glu tca gag agt gaa ggt ctg aaa ccc aag gaa gag gcc cca cct gca ggg Ser Glu Ser Glu Gly Leu Lys Pro Lys Glu Glu Ala Pro Pro Ala Gly gga cag agt gtg gtc caa gaa aca ttc agc aaa aac ttc att tgc aat Gly Gln Ser Val Val Gln Glu Thr Phe Ser Lys Asn Phe Ile Cys Asn gtc tgt gaa tcg cct ttt ctt tcc att aaa gac cta acc aaa cat tta Val Cys Glu Ser Pro Phe Leu Ser Ile Lys Asp Leu Thr Lys His Leu

| tcc gtc cat gct Ser Val His Ala 1145 | | | | |
|--|-------------|-------------|---------------|---|
| ctg ttt aag gtt Leu Phe Lys Val 1160 | | Leu Ser Glu | - | - |
| ggg gtt gga aat Gly Val Gly Asn 1175 | | | | _ |
| ttc tta tgc aat Phe Leu Cys Asn | | | Asp Leu His P | |
| gta tgc aca cac Val Cys Thr His 1210 | His Glu Phe | | Thr Leu Arg P | |
| ttc aca gac ccc Phe Thr Asp Pro 1225 | | | | |
| gaa gag cct tta Glu Glu Pro Leu 1240 | - | Arg Glu Glu | = : | |
| gaa gag ctt tac Glu Glu Leu Tyr 1255 | | | | |
| aag gat cca gat Lys Asp Pro Asp | | | Gln His Tyr P | |
| aaa cct cct cca Lys Pro Pro Pro 1290 | Phe Gln Tyr | | Asn Pro Met G | |
| gtg aca gcc acc Val Thr Ala Thr 1305 | | | | |
| act gcc atc cgc Thr Ala Ile Arg 1320 | | Cys Gly Lys | | |
| gag ctg cat aag Glu Leu His Lys 1335 | | | | |

| agg tac acc cct Arg Tyr Thr Pro | | | Leu Lys Gln Ti | |
|--|--|--|--|---|
| ccc aaa aat gga Pro Lys Asn Gly 137 | Val Val Val | _ | Ser Gly Lys As | |
| aga cgg atg ggg Arg Arg Met Gly 1385 | Gln Pro Lys | | | |
| aaa atg tct cca Lys Met Ser Pro 1400 | | Lys Leu Ser | | |
| cag ctg gtg cag Gln Leu Val Gln 1415 | | Leu Gln Lys | | |
| aag gcg gac ctg Lys Ala Asp Leu | | | Ser Ser His I | |
| tac tgt gac agg Tyr Cys Asp Arg 145 | Glu Phe Thr | | Ser Leu Asn Ly | |
| gcc ttc agc tgt Ala Phe Ser Cys 1465 | | | | |
| tcc cat tcg tct Ser His Ser Ser | | | tca tct tct ag | |
| 1480 | 1485 | | Ser Ser Ser Se 1490 | er Ser Asp |
| aga aac agc agc Arg Asn Ser Ser 1495 | 1485 | cgg agg cgg Arg Arg Arg | 1490 act gca gat ac | cc gag atc 4686 |
| aga aac agc agc Arg Asn Ser Ser | tgc cac ccc Cys His Pro 1500 acg cag gca | cgg agg cgg Arg Arg Arg | 1490 act gca gat ac Thr Ala Asp Th 1505 aag acc aga gc Lys Thr Arg A | cc gag atc 4686 nr Glu Ile 1510 ct cgg agt 4734 |
| aga aac agc agc Arg Asn Ser Ser 1495 aag atg cag agc | tgc cac ccc Cys His Pro 1500 acg cag gca Thr Gln Ala 1515 cag gcc tca Gln Ala Ser | cgg agg cgg Arg Arg Arg ccc ttg ggc Pro Leu Gly 1520 ctg ccc tcc | 1490 act gca gat ac Thr Ala Asp Th 1505 aag acc aga gc Lys Thr Arg Al tcg tcc ttc ac Ser Ser Phe Ar | cc gag atc 4686 ar Glu Ile 1510 ct cgg agt 4734 la Arg Ser 1525 ga tcc aga 4782 |
| aga aac agc agc Arg Asn Ser Ser 1495 aag atg cag agc Lys Met Gln Ser aca ggc ccc gcc Thr Gly Pro Ala | tgc cac ccc Cys His Pro 1500 acg cag gca Thr Gln Ala 1515 cag gcc tca Gln Ala Ser ttt gca gct Phe Ala Ala | cgg agg cgg Arg Arg Arg ccc ttg ggc Pro Leu Gly 1520 ctg ccc tcc Leu Pro Ser 1535 tca gtg aaa | 1490 act gca gat ac Thr Ala Asp Th 1505 aag acc aga gc Lys Thr Arg Al tcg tcc ttc ac Ser Ser Phe Ar 15 | cc gag atc 4686 ar Glu Ile 1510 ct cgg agt 4734 a Arg Ser 1525 ga tcc aga 4782 ag Ser Arg 540 ca agc tct 4830 |

| Ser Ser Leu Arg Asn Ser Ser Pro Ile Arg Met Ala Lys Ile Thr His 1560 1565 1570 |
|--|
| gtc gag ggc aaa aaa ccc aaa gct gtt gcc aag agt cat tct gct cag 4926 Val Glu Gly Lys Lys Pro Lys Ala Val Ala Lys Ser His Ser Ala Gln 1575 1580 1585 1590 |
| ctc tca agc aaa tcc tcc cga ggc ctg cat gtc aga gtg cag aag agc 4974 Leu Ser Ser Lys Ser Ser Arg Gly Leu His Val Arg Val Gln Lys Ser 1595 1600 1605 |
| aaa get gte ata cag age aag act gee etg gee agt aag agg aga aca 5022 Lys Ala Val Ile Gln Ser Lys Thr Ala Leu Ala Ser Lys Arg Arg Thr 1610 1615 1620 |
| gac cgg ttc ata gtg aaa tct aga gag cgc agc ggg ggc cca atc acc Asp Arg Phe Ile Val Lys Ser Arg Glu Arg Ser Gly Gly Pro Ile Thr 1625 1630 1635 |
| cga agc ctt cag ctg gca gct gct gcg gac ctg agt gaa agc agg aga 5118 Arg Ser Leu Gln Leu Ala Ala Ala Ala Asp Leu Ser Glu Ser Arg Arg 1640 1645 1650 |
| gag gac agc agt gcc agg cat gag ctg aag gac ttc agc tac agt ctc 5166 Glu Asp Ser Ser Ala Arg His Glu Leu Lys Asp Phe Ser Tyr Ser Leu 1655 1660 1665 1670 |
| cgc ctg gca tct cga tgc ggc tca tca aca gcc tct tac atc acc aga 5214 Arg Leu Ala Ser Arg Cys Gly Ser Ser Thr Ala Ser Tyr Ile Thr Arg 1675 1680 1685 |
| caa tgc aga aag gtc aag gcc gcc gca gca act ccg ttc cag gga ccc 5262 Gln Cys Arg Lys Val Lys Ala Ala Ala Ala Thr Pro Phe Gln Gly Pro 1690 1695 1700 |
| ttc ctc aaa gag taggcactct gtctgctcct taacagcacc tgaagtgacc 5314 Phe Leu Lys Glu 1705 |
| tggaatcagt gaagccaaag ggaccagcag tetgeeetge agagagcaet gaceteteee 5374 agttgtgaga gtgagagaac gagagagaa gagagagaa gagagagaa gagagaga |
| aagaagcagt gttttgggac gatagggtgg aggcgtgcct actttgtctc ctctggtggg 6094 acctcctaca tcattggcat ctgaaccttg caagttcgct gcaaagagaa gcaaaggaaa 6154 |

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<212> PRT

<213> Rattus SP.

aaaaaaaaa aaaaaaa

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Met His Gln Asn Thr Glu Ser Val Ala Ala Thr Glu Thr Leu Ala Glu
1 5 10 15

Val Pro Glu His Val Leu Arg Gly Leu Pro Glu Glu Val Arg Leu Phe
20 25 30

Pro Ser Ala Val Asp Lys Thr Arg Ile Gly Val Trp Ala Thr Lys Pro 35 40 45

Ile Leu Lys Gly Lys Lys Phe Gly Pro Phe Val Gly Asp Lys Lys 50 55 60

Arg Ser Gln Val Arg Asn Asn Val Tyr Met Trp Glu Val Tyr Tyr Pro
65 70 75 80

Asn Leu Gly Trp Met Cys Ile Asp Ala Thr Asp Pro Glu Lys Gly Asn 85 90 95

Trp Leu Arg Tyr Val Asn Trp Ala Cys Ser Gly Glu Glu Gln Asn Leu 100 105 110

Phe Pro Leu Glu Ile Asn Arg Ala Ile Tyr Tyr Lys Thr Leu Lys Pro 115 120 125

Ile Ala Pro Gly Glu Glu Leu Leu Val Trp Tyr Asn Gly Glu Asp Asn 130 135 140

Pro Glu Ile Ala Ala Ile Glu Glu Glu Arg Ala Ser Ala Arg Ser 145 150 155 160

Lys Arg Ser Ser Pro Lys Ser Arg Arg Gly Lys Lys Lys Ser His Glu 165 170 175

Asn Lys Asn Lys Gly Ile Arg Thr His Pro Thr Gln Leu Lys Ala Ser 180 185 190

Glu Leu Asp Ser Thr Phe Ala Asn Met Arg Gly Ser Ala Glu Gly Pro 195 200 205

Lys Glu Glu Asp Glu Arg Pro Leu Ala Ser Ala Pro Glu Gln Pro Ala 210 215 220

Pro Leu Pro Glu Val Gly Asn Gln Asp Ala Val Pro Gln Val Ala Ile 225 230 235 240

Pro Leu Pro Ala Cys Glu Pro Gln Pro Glu Val Asp Gly Lys Gln Glu
245 250 255

Val Thr Asp Cys Glu Val Asn Asp Val Glu Glu Glu Glu Leu Glu Glu Glu 260

Glu Glu Glu Leu Glu Glu Glu Glu Glu Glu Leu Gly Glu Asp Gly
275 280 285

Val Glu Glu Ala Asp Met Pro Asn Glu Ser Ser Ala Lys Glu Pro Glu 290 295 300

Ile Arg Cys Glu Glu Lys Pro Glu Asp Leu Leu Glu Glu Pro Gln Ser

305 310 315 320 Met Ser Asn Glu Ala Arg Glu Asp Ser Pro Asp Val Thr Pro Pro Pro

325 330 335 His Thr Pro Arg Ala Arg Glu Glu Ala Asn Gly Asp Val Leu Glu Thr

340 345 350
Phe Met Phe Pro Cys Gln His Cys Glu Arg Lys Phe Ala Thr Lys Gln

Fuster Feet a commence

360 Gly Leu Glu Arg His Met His Ile His Ile Ser Thr Ile Asn His Ala 375 380 Phe Lys Cys Lys Tyr Cys Gly Lys Arg Phe Gly Thr Gln Ile Asn Arg 390 395 Arg Arg His Glu Arg Arg His Glu Thr Gly Leu Lys Arg Arg Pro Ser 410 Met Thr Leu Gln Ser Ser Glu Asp Pro Asp Asp Gly Lys Gly Glu Asn 425 420 Val Thr Ser Lys Asp Glu Ser Ser Pro Pro Gln Leu Gly Gln Asp Cys 440 435 Leu Ile Leu Asn Ser Glu Lys Thr Ser Gln Glu Val Leu Asn Ser Ser 455 Phe Val Glu Glu Asn Gly Glu Val Lys Glu Leu His Pro Cys Lys Tyr 470 475 Cys Lys Lys Val Phe Gly Thr His Thr Asn Met Arg Arg His Gln Arg 485 490 Arg Val His Glu Arg His Leu Ile Pro Lys Gly Val Arg Arg Lys Gly 505 Gly Leu Leu Glu Glu Pro Gln Pro Pro Ala Glu Gln Ala Pro Pro Ser 520 Gln Asn Val Tyr Val Pro Ser Thr Glu Pro Glu Glu Glu Gly Glu Thr 535 Asp Asp Val Tyr Ile Met Asp Ile Ser Ser Asn Ile Ser Glu Asn Leu 555 Asn Tyr Tyr Ile Asp Gly Lys Ile Gln Thr Asn Ser Ser Thr Ser Asn 570 Cys Asp Val Ile Glu Met Glu Ser Asn Ser Ala His Leu Tyr Gly Ile 585 Asp Cys Leu Leu Thr Pro Val Thr Val Glu Ile Thr Gln Asn Ile Lys 595 600 Ser Thr Gln Val Ser Val Thr Asp Asp Leu Leu Lys Asp Ser Pro Ser 615 Ser Thr Asn Cys Glu Ser Lys Lys Arg Arg Thr Ala Ser Pro Pro Val 635 630 Leu Pro Lys Ile Lys Thr Glu Thr Glu Ser Asp Ser Thr Ala Pro Ser 645 650 Cys Ser Leu Ser Leu Pro Leu Ser Ile Ser Thr Ala Glu Val Val Ser 660 665 Phe His Lys Glu Lys Gly Val Tyr Leu Ser Ser Lys Leu Lys Gln Leu 680 Leu Gln Thr Gln Asp Lys Leu Thr Leu Pro Ala Gly Phe Ser Ala Ala 6.95 700 Glu Ile Pro Lys Leu Gly Pro Val Cys Ala Ser Ala Pro Ala Ser Met 715 710 Leu Pro Val Thr Ser Ser Arg Phe Lys Arg Arg Thr Ser Ser Pro Pro 725 730 Ser Ser Pro Gln His Ser Pro Ala Leu Arg Asp Phe Gly Lys Pro Asn 745 Asp Gly Lys Ala Ala Trp Thr Asp Thr Val Leu Thr Ser Lys Lys Pro 760 Lys Leu Glu Ser Arg Ser Asp Ser Pro Ala Trp Ser Leu Ser Gly Arg 770 775

Asp Glu Arq Glu Thr Gly Ser Pro Pro Cys Phe Asp Glu Tyr Lys Ile 790 795 Ser Lys Glu Trp Ala Ala Ser Ser Thr Phe Ser Ser Val Cys Asn Gln 805 810 Gln Pro Leu Asp Leu Ser Ser Gly Val Lys Gln Lys Ser Glu Gly Thr 825 820 Gly Lys Thr Pro Val Pro Trp Glu Ser Val Leu Asp Leu Ser Val His 840 Lys Lys Pro Cys Asp Ser Glu Gly Lys Glu Phe Lys Glu Asn His Leu Ala Gln Pro Ala Ala Lys Lys Lys Pro Thr Thr Cys Met Leu Gln 870 875 Lys Val Leu Leu Asn Glu Tyr Asn Gly Val Ser Leu Pro Thr Glu Thr 890 885 Thr Pro Glu Val Thr Arg Ser Pro Ser Pro Cys Lys Ser Pro Asp Thr 905 900 Gln Pro Asp Pro Glu Leu Gly Pro Asp Ser Ser Cys Ser Val Pro Thr 920 Ala Glu Ser Pro Pro Glu Val Val Gly Pro Ser Ser Pro Pro Leu Gln 935 940 Thr Ala Ser Leu Ser Ser Gly Gln Leu Pro Pro Leu Leu Thr Pro Thr 950 955 Glu Pro Ser Ser Pro Pro Pro Cys Pro Pro Val Leu Thr Val Ala Thr 970 965 Pro Pro Pro Leu Leu Pro Thr Val Pro Leu Ser His Pro Ser Ser 985 980 Asp Ala Ser Pro Gln Gln Cys Pro Ser Pro Phe Ser Asn Thr Thr Ala 1000 1005 Gln Ser Pro Leu Pro Ile Leu Ser Pro Thr Val Ser Pro Ser Pro Ser 1015 1020 Pro Ile Pro Pro Val Glu Pro Leu Met Ser Ala Ala Ser Pro Gly Pro 1035 . 1040 1030 Pro Thr Leu Ser Ser Ser Ser Ser Ser Ser Ser Phe Pro Ser Ser 1045 1050 Ser Cys Ser Ser Thr Ser Pro Ser Pro Pro Pro Leu Ser Ala Val Ser 1065 1070 Ser Val Val Ser Ser Gly Asp Asn Leu Glu Ala Ser Leu Pro Ala Val 1075 1080 1085 Thr Phe Lys Gln Glu Glu Ser Glu Ser Glu Gly Leu Lys Pro Lys Glu 1095 Glu Ala Pro Pro Ala Gly Gly Gln Ser Val Val Gln Glu Thr Phe Ser 1110 1115 Lys Asn Phe Ile Cys Asn Val Cys Glu Ser Pro Phe Leu Ser Ile Lys 1125 1130 Asp Leu Thr Lys His Leu Ser Val His Ala Glu Glu Trp Pro Phe Lys 1145 1140 Cys Glu Phe Cys Val Gln Leu Phe Lys Val Lys Thr Asp Leu Ser Glu 1160 His Arg Phe Leu Leu His Gly Val Gly Asn Ile Phe Val Cys Ser Val 1175 1180 Cys Lys Lys Glu Phe Ala Phe Leu Cys Asn Leu Gln Gln His Gln Arg 1190 1195 Asp Leu His Pro Asp Glu Val Cys Thr His His Glu Phe Glu Ser Gly

1205 1210 Thr Leu Arg Pro Gln Asn Phe Thr Asp Pro Ser Lys Ala Asn Val Glu 1225 His Met Pro Ser Leu Pro Glu Glu Pro Leu Glu Thr Ser Arg Glu Glu 1240 1245 Glu Leu Asn Asp Ser Ser Glu Glu Leu Tyr Thr Thr Ile Lys Ile Met 1255 Ala Ser Gly Ile Lys Thr Lys Asp Pro Asp Val Arg Leu Gly Leu Asn 1270 1275 Gln His Tyr Pro Ser Phe Lys Pro Pro Pro Phe Gln Tyr His His Arg 1285 1290 Asn Pro Met Gly Ile Gly Val Thr Ala Thr Asn Phe Thr His Asn 1300 1305 Ile Pro Gln Thr Phe Thr Thr Ala Ile Arg Cys Thr Lys Cys Gly Lys 1315 1320 1325 Gly Val Asp Asn Met Pro Glu Leu His Lys His Ile Leu Ala Cys Ala 1335 1340 Ser Ala Ser Asp Lys Lys Arg Tyr Thr Pro Lys Lys Asn Pro Val Pro 1350 1355 Leu Lys Gln Thr Val Gln Pro Lys Asn Gly Val Val Leu Asp Asn 1365 1370 Ser Gly Lys Asn Ala Phe Arg Arg Met Gly Gln Pro Lys Arg Leu Ser 1380 1385 Phe Asn Val Glu Leu Gly Lys Met Ser Pro Asn Lys Leu Lys Leu Ser 1400 Ala Leu Lys Lys Lys Asn Gln Leu Val Gln Lys Ala Ile Leu Gln Lys 1415 1420 Asn Arg Ala Ala Lys Gln Lys Ala Asp Leu Arg Asp Thr Ser Glu Ala 1430 1435 Ser Ser His Ile Cys Pro Tyr Cys Asp Arg Glu Phe Thr Tyr Ile Gly 1445 1450 Ser Leu Asn Lys His Ala Ala Phe Ser Cys Pro Lys Lys Pro Leu Ser 1465 Pro Ser Lys Arg Lys Val Ser His Ser Ser Lys Lys Gly Gly His Ala 1480 Ser Ser Ser Ser Ser Asp Arg Asn Ser Ser Cys His Pro Arg Arg Arg 1495 1500 Thr Ala Asp Thr Glu Ile Lys Met Gln Ser Thr Gln Ala Pro Leu Gly 1510 1515 Lys Thr Arg Ala Arg Ser Thr Gly Pro Ala Gln Ala Ser Leu Pro Ser 1530 1525 Ser Ser Phe Arg Ser Arg Gln Asn Val Lys Phe Ala Ala Ser Val Lys 1545 1540 Ser Lys Lys Ala Ser Ser Ser Ser Leu Arg Asn Ser Ser Pro Ile Arg 1560 1565 1555 Met Ala Lys Ile Thr His Val Glu Gly Lys Lys Pro Lys Ala Val Ala 1575 Lys Ser His Ser Ala Gln Leu Ser Ser Lys Ser Ser Arg Gly Leu His 1590 1595 Val Arg Val Gln Lys Ser Lys Ala Val Ile Gln Ser Lys Thr Ala Leu 1610 Ala Ser Lys Arg Arg Thr Asp Arg Phe Ile Val Lys Ser Arg Glu Arg 1620 1625

 Ser Gly Gly Pro Ile Thr Arg Ser Leu Gln Leu Ala Ala Ala Ala Ala Asp
 1635
 1640
 1645

 Leu Ser Glu Ser Arg Arg Glu Asp Ser Ser Ala Arg His Glu Leu Lys
 1650
 1655
 1660

 Asp Phe Ser Tyr Ser Leu Arg Leu Ala Ser Arg Cys Gly Ser Ser Thr
 1665
 1670
 1675
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 Ala Ser Tyr Ile Thr Arg Gln Cys Arg Lys Val Lys Ala Ala Ala Ala Ala
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 Thr Pro Phe Gln Gly Pro Phe Leu Lys Glu
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<212> DNA
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<222> (121)...(5277)

<400> 3

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gag gta ccc gaa cat gtg ctg cga gga ctt ccg gag gaa gtg agg ctt 216 Glu Val Pro Glu His Val Leu Arg Gly Leu Pro Glu Glu Val Arg Leu 20 25 30

ttc cct tct gct gtt gac aag acc cgg att ggt gtc tgg gcc act aaa 264
Phe Pro Ser Ala Val Asp Lys Thr Arg Ile Gly Val Trp Ala Thr Lys
35 40 45

cca att tta aaa ggg aaa aaa ttt ggg cca ttt gtt ggt gat aag aaa 312 Pro Ile Leu Lys Gly Lys Lys Phe Gly Pro Phe Val Gly Asp Lys Lys

aaa aga tct cag gtt aag aat aat gta tac atg tgg gag gtg tat tac
Lys Arg Ser Gln Val Lys Asn Asn Val Tyr Met Trp Glu Val Tyr Tyr
65 70 75 80

cca aat ttg gga tgg atg tgc att gat gcc act gat cca gag aag gga 408
Pro Asn Leu Gly Trp Met Cys Ile Asp Ala Thr Asp Pro Glu Lys Gly
85 90 95

aac tgg ctg cga tat gtg aat tgg gct tgc tca gga gaa gag caa aat 456 Asn Trp Leu Arg Tyr Val Asn Trp Ala Cys Ser Gly Glu Glu Gln Asn 100 105 110

tta ttc cca ctg gaa atc aac aga gcc att tac tat aaa act tta aag 504

| Leu | Phe | Pro 115 | Leu | Glu | Ile | Asn | Arg 120 | Ala | Ile | Tyr | Tyr | Lys 125 | Thr | Leu | Lys | |
|-----|-----|------------|-----|-----|-----|-----|------------|-------------------|-----|-----|-----|------------|-----|-----|-----|------|
| | | | _ | | | | | ctg Leu | - | | | | | _ | _ | 552 |
| | | | | - | _ | | | gag Glu | | _ | | | | | | 600 |
| _ | _ | | - | | | _ | - | cgg Arg | | | _ | | | | | 648 |
| _ | | | | | | | | atc Ile 185 | | _ | | | _ | _ | | 696 |
| _ | | | _ | | | | _ | aat Asn | | _ | | | | | | 744 |
| | | | | | | | | tca Ser | | | | | | | | 792 |
| _ | | | _ | _ | _ | _ | _ | cag Gln | | | | | | | | 840 |
| | | _ | | _ | | | | cag Gln | | _ | | - | | _ | | 888 |
| | | | | | | | | gat Asp 265 | | | | | | | | 936 |
| | | | | | | | | gaa Glu | | | | | | | | 984 |
| _ | _ | _ | | | _ | _ | _ | gcc Ala | _ | _ | | | - | | | 1032 |
| | | | | _ | | | _ | gat Asp | | | | | | | | 1080 |
| | _ | | | | | | _ | gaa Glu | | | _ | _ | _ | | | 1128 |

| _ | | - | _ | caa Gln | | | _ | | | _ | | _ | | _ | 1176 |
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| | - | | | tct Ser 470 | | - | | | | | | | | | 1560 |
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| | | | | cag Gln | | | | | | | | | | | 1656 |
| | | | | aaa Lys | | | | | | | | | | | 1704 |
| | | | | acc Thr | | | | | | | | | | | 1752 |

File and the contraction of the

| | | - | | | - | - | - | | | | | - | | tct Ser | | 1800 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-------------------|---|------|
| | | | _ | | | | | | | - | | | | caa Gln 575 | | 1848 |
| | | | | _ | | - | _ | | | | _ | | | gct Ala | _ | 1896 |
| _ | _ | | | | | | _ | _ | | | | _ | | gtg Val | • | 1944 |
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| - | | | | _ | | - | | | | | | | | tgt Cys | | 2280 |
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| Gln | Leu | Pro | Pro | Leu 965 | Leu | Ile | Pro | Thr | Asp 970 | Pro | Ser | Ser | Pro | Pro 975 | Pro | |
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| • | aca gat ccc Thr Asp Pro 5 | | | | | 3864 |
| | gat cct tta Asp Pro Leu | - | Lys Glu G | | - | 3912 |
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| | acc gcc att Thr Ala Ile | | Lys Cys C | | _ | 4152 |
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| aaa aaa aat cag Lys Lys Asn Gln 1425 | | | _ | | 440 |
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| atc tgc cct tac Ile Cys Pro Tyr 146 | Cys Asn Arg | | | | 536 |
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